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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Norman BITTERLICH
Serial No.	:	10/009,125
Filed	:	December 5, 2001
For	:	METHOD FOR DETERMINING SIGNIFICANT LOSSES IN BONE DENSITY
Group Art Unit	:	UNKNOWN
Examiner	:	UNKNOWN

Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Preliminary to examination, please amend the above-identified patent application as follows:

IN THE CLAIMS:

Amend claims 1-5 as follows, the amendments being shown by brackets and underlining in an Appendix hereto:

1. (Amended) A method for determining any significant bone density loss in a human patient, comprising storing in an electronic storage medium as reference values measurement values of real or mathematically simulated bone

density loss processes, as a function of time, the measurement values being of medically accepted practical or theoretical clinical signs and symptoms of bone density loss, measuring bone marker values of serum or urine samples of the patient associated with bone density losses,

recording the bone marker values over an input mask in an electronic data memory, and, by the following steps, processing the bone marker values relative to the reference values thereby to determine any significant bone density loss in the patient:

a) at the time of the analysis, copying all N available measured bone marker values M of the patient which were measured at times $t_1 \ldots t_n$ from the data memory over an interrogation function thereby to make the measured values available for further processing, measured bone marker values M (t_n; k) of K in the laboratory being determined after step x of the process at times $t_1 \ldots t_n$,

b) normalizing the measured values of the bone markers with respect to a first line in a table according to the equation

$$M^*(t_n;k) = \frac{M(t_n;k) - M(t_1;k)}{M(t_1;k)} \qquad k = 1,\ldots,K; \quad n = 1,\ldots,N$$

and converting the measurements as a function of time into months,

c) the normalized measured value being converted into a scalar quantity $D(t_n)$ for a graduated description of the course of the bone density, the equation

$$D(t_n) = \sqrt{\sum_{k=1}^{K} Wk \cdot \left(M^*(t_n;k)\right)^2}$$

defining the graduated description of the course of the relationship

d) from the evaluations of the progress determined, calculating by interpolation evaluations of the progress for those time sections of

$$D^*(t) = \frac{(t_n - t) \cdot D(n-1) + (t - t_{n-1}) \cdot D(n)}{t_n - t_{n-1}} \quad , t \in \left[t_{n-1}, t_n\right]$$

for which reference values are available,

e) from the interpolated evaluations of the progress, calculating similarity dimensions between the data by means of the function

$$A_j(t) = \sum_{m=1}^{M} \frac{t_m}{t_M} \cdot V_m \cdot \left(R_j(t_m - D^*(t_m)\right)^2$$

said function of this paragraph (e) being used to calculate a similarity dimension between the data, which is to be investigated, and all the

reference values, available in the database and, at the same time, similarity dimensions to the reference values and to the time in months being found,

f) from the similarity dimensions for all reference values, determining those reference values which have a high similarity in the mathematical sense, as follows:

greatest similarity: $$A^* = \min_{j=1,\ldots,J}\{A_j\}$$

positive alternative (+) $$A^+ = \min_{j=1,\ldots,J,\, A_j \neq A^*,\, R_j(IN) > I(IN)}\{A_j\}$$

negative alternative (-) $$A^- = \min_{j=1,\ldots,J,\, A_j \neq A^*,\, R_j(IN) < I(IN)}\{A_j\}$$

with subsequent output of the type description as text component for describing the situation;

g) deriving a predicted value from the three reference values of paragraph (f), if $B_1 = A^*$, $B_2 = A^+$, $B_3 = A^-$,

the following expression

$$R(t) = \frac{1}{\sum_{i=1}^{3} B_i} \cdot \sum_{j=1}^{3}\left(\left(\sum_{i=1}^{3} B_i - B_j\right) \cdot R_j(t)\right)$$

being used for the predicted value at time t;

h) optimizing quantitative prediction of the bone density loss by assigning standard specifications to degrees of freedom given as functional parameters in the functional relation of $D(t_n)$ and $A_j(t)$ and fitting by statistical analysis of the reference values to practical experience; and

i) calculating the time at which, according to said quantitative prediction the percentage deviation is greater than a specified threshold value, this time being the starting point for planning scheduling of a next investigation.

2. (Amended) The method of claim 1, wherein the degrees of freedom, given as function parameters in the functional relationship of $D(t_n)$ and $A_j(t)$, are filled in by the mathematical method of least squares so that specified sequences are taken into consideration in a best way for reference values.

3. (Amended) The method of claim 1, wherein the reference values are calculated values from an analytical mathematically assumed course of bone density loss.

4. (Amended) The method of claim 1, wherein the reference values empirical values from imaginary, assumed processes.

5. (Amended) The method of claim 1, wherein the reference values are concrete values from patients with known amounts of loss of bone density.

REMARKS

These formal amendments, which do not involve new matter, place the claims in better condition for examination.

Respectfully submitted,

Jordan and Hamburg LLP

By___________________________

C. Bruce Hamburg
Reg. No. 22,389
Attorney for Applicant

122 East 42nd Street
New York, New York 10168
(212) 986-2340

APPENDIX I

AMENDED CLAIMS WITH AMENDMENTS INDICATED THEREIN
BY BRACKETS AND UNDERLINING

1. (Amended) A method for determining any significant bone density [losses] loss in a human patient, [wherein] comprising storing in an electronic storage medium as reference values measurement values of real or mathematically simulated bone density loss processes[, which are present in electronic storage media and], as a function of time, [reflect laboratory parameters] the measurement values being of [practically or theoretically known] medically accepted practical or theoretical clinical signs and symptoms[, are used as reference values for the process] of bone density loss, [and] measuring bone marker values of serum or urine samples[,] of the patient associated with bone density losses, [and measured by common laboratory techniques, are determined by sample preparation steps such as

- treating with antibodies
- incubation steps
- separation procedures
- using analytical techniques]

[and recorded] recording the bone marker values over an input mask in an electronic data memory, [are used for determining] and, by the following steps,

processing the bone marker values relative to the reference values thereby to determine any significant bone density [losses,] loss in the patient:

a) at the time of the analysis, copying all N available [patient-related data being copied] measured bone marker values M of the patient which were measured at times $t_1 \ldots t_n$ from the data memory over an interrogation function [and made] thereby to make the measured values available for [the] further processing, [(]measured bone marker values M (t_n; k) of [the] K in the laboratory [of the bone marker,] being determined after step x of the process at times $t_1 \ldots t_n$[)],

b) normalizing the measured values of the bone markers with respect to [the] a first line in [the Table being normalized] a table according to the equation

$$M^*(t_n;k) = \frac{M(t_n;k) - M(t_1;k)}{M(t_1;k)} \qquad k = 1,\ldots,K; \quad n = 1,\ldots,N$$

and converting the measurements as a function of time [being converted] into months,

c) the normalized measured value being converted into a scalar quantity $D(t_n)$ for [the] a graduated description of the course of the bone density, the equation

$$D(t_n) = \sqrt{\sum_{k=1}^{K} Wk \cdot \left(M^*(t_n;k)\right)^2}$$

[being used for] <u>defining</u> the graduated description of the course of the relationship

d) from the evaluations of the progress determined, <u>calculating by interpolation</u> evaluations of the progress for those time sections of

$$D^*(t)=\frac{(t_n-t)\cdot D(n-1)+(t-t_{n-1})\cdot D(n)}{t_n-t_{n-1}} \quad ,t\in\left[t_{n-1},t_n\right]$$

[being calculated by interpolation,] for which reference values are available,

e) from the interpolated evaluations of the progress, <u>calculating</u> similarity dimensions [being calculated,] <u>between the data by means of</u> the function

$$A_j(t)=\sum_{m=1}^{M}\frac{t_m}{t_M}\cdot V_m\cdot\left(R_j(t_m-D^*(t_m)\right)^2$$

<u>said function of this paragraph (e)</u> being used to calculate a similarity dimension between the data, which is to be investigated, and all the reference values, available in the database and, at the same time, similarity dimensions to the reference values and to the time in months being found,

f) from the similarity dimensions for all reference values, determining those reference values [being determined,] which have a high similarity in the mathematical sense, as follows: [such as the]

greatest similarity: $A^* = \min\limits_{j=1,\dots,J}\{A_j\}$

positive alternative (+) $A^+ = \min\limits_{j=1,\dots,J,\,A_j \neq A^*,\,R_j(t_N) > L(t_N)}\{A_j\}$

negative alternative (-) $A^- = \min\limits_{j=1,\dots,J,\,A_j \neq A^*,\,R_j(t_N) < L(t_N)}\{A_j\}$

with subsequent output of the type description as text component for describing the situation;

g) [the prediction being derived from these] deriving a predicted value from the three reference values of paragraph (f), if $B_1 = A^*$, $B_2 = A^+$, $B_3 = A^-$, the following expression

$$R(t) = \frac{1}{\sum_{i=1}^{3} B_i} \cdot \sum_{j=1}^{3}\left(\left(\sum_{i=1}^{3} B_i - B_j\right) \cdot R_j(t)\right)$$

being used for the predicted value at time t;

h) [the] optimizing quantitative prediction of the bone density loss by assigning standard specifications to degrees of freedom [for the specification of the model,] given as functional parameters in the

functional relation of $D(t_n)$ and $A_j(t)$ [being occupied by standard specifications] and [fitted] fitting by statistical analysis of the reference values to practical experience [for optimizing the quantitative prediction of the bone density loss]; and

i) calculating the time [being calculated,] at which, according to [this] said quantitative prediction [strategy,] the percentage deviation is greater than a specified threshold value, this time being the starting point for planning [the] scheduling of [the] a next investigation.

2. (Amended) The method of claim 1, wherein the degrees of freedom, given as function parameters in the functional relationship of $D(t_n)$ and $A_j(t)$, are filled in by the mathematical method of least squares so that specified sequences are taken into consideration in [the] a best way for reference values.

3. (Amended) The method of claim 1, wherein the reference values are [used, which are] calculated values from an analytical mathematically assumed course [(exponential functions)] of bone density loss.

4. (Amended) The method of claim 1, wherein the reference values [are used, which are] empirical values from imaginary, assumed processes.

5. (Amended) The method of claim 1, wherein the reference values are [used, which are] concrete values from patients with known [situations] amounts of loss of bone density.